Tobacco Dependence as a Chronic Disease

Therese Shumaker, MA, RDN, NCTTP
It’s easy to quit smoking
I’ve done it 1000 times!

Mark Twain
Tobacco Dependence Is A Chronic Disease

- Identifiable etiology and pathophysiology
- Symptoms
- Characterized by relapses and remissions
- Spectrum of disease severity
- Effective treatments exist
- Variety of treatment options
- May require referral to specialists
- Individualized therapy is important
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Carcinogenicity of Tobacco Smoke

• Cigarette smoking is the single largest preventable cause of death and disability in developed countries

• Tobacco smoke contains >7000 chemicals

• >60 carcinogens are in cigarette smoke, and a minimum of 16 are in unburned tobacco

• The composition of processed tobacco in cigarettes influences the chemistry and toxicity of the smoke

https://www.youtube.com/watch?v=snxwen68gxY

Surgeon General's Report, 1989
28 Known Carcinogens in smokeless tobacco

**Including**

- β-Angelica lactone
- Coumarin
- Ethyl carbamate (urethane)
- Formaldehyde
- Acetaldehyde
- Crotonaldehyde
- Tobacco-specific N-nitrosamines (TSNA)
  - N'-Nitrosonornicotine (NNN)
  - 4-(Methylnitrosamino)-1-(3-pyridyl)-1-butanone (NNK)
  - 4-(Methylnitrosamino)-1-(3-pyridyl)-1-butanol (NNAL)
  - N'-Nitrosoanabasine (NAB)
- Arsenic
- Nickel compounds
- Polonium-210
- Uranium-235
- Uranium-238

Ventral Tegmental Area and Nucleus Accumbens Are Primary Locations for Core Pleasure Experiences
Nicotine - the “why” people smoke

• Nicotine – highly addictive substance
• Not a carcinogen
• Liquid in its native state
• Distilled from burning tobacco and carried on tar droplets
• Brain chemistry changes
• Half-Life 90-120 minutes
• Reaches the brain in 7-10 seconds
Pharmacology of Nicotine

• Enhanced release of many CNS neurotransmitters
• Peripheral release of norepinephrine
• Sympathetic activation
• Behavioral arousal; increased vigilance; reduced anxiety
A Key to the Reinforcing (Addictive) Effects of Nicotine (and other Psychostimulants)

Dopamine

*A quantitative relationship between levels of dopamine receptor occupancy by dopamine and high “intensity.”

Volkow et al: J Pharmacol Exp Ther 291:409, 1999
Dopamine Release

- Diverse agents all increase extracellular dopamine (DA) levels in the shell of the nucleus accumbens (NAc)
  - Opioids
  - Stimulants
  - Alcohol
  - Nicotine
  - Marijuana

- Natural rewards also increase DA levels
  - Sex
  - Food
  - Water

Effects of Drugs on Dopamine Levels

Di Chiara and Imperato: Proceedings of the National Academy of Sciences USA, 1988; courtesy of Nora D Volkow, MD
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Withdrawal Symptoms (DSM-5)

- Irritability, frustration, or anger
- Anxiety
- Difficulty concentrating
- Increased appetite
- Restlessness
- Depressed mood
- Insomnia
Drug Craving

Anticipated reward not delivered

Chronic drug exposure depletes dopamine

Dopamine hypoactivity

Drug craving

Cycle of Addiction

Drug Euphoria
Positive reinforcement
Activated reward pathways

Drug administration
Drug-seeking behavior
Failed impulse suppression

Neuroadaptation
Withdrawal/tolerance
Protracted hedonic dysregulation

Drug craving
Negative reinforcement
Dysregulated reward pathways

Drug-related cues

Conceptualizing Addiction

- Disease of brain reward centers
- Addictive drugs “hijack” brain circuits that promote survival and influence rational thought
- Changes the brain chemistry

Addiction As a Brain Disease – ASAM

Addiction is a primary, chronic disease of brain reward, motivation, memory and related circuitry

• Dysfunction in these circuits leads to characteristic biological, psychological, social and spiritual manifestations

• Pursuit of reward and/or relief by substance use and other behaviors

• Characterized by impairment in behavioral control, craving, inability to consistently abstain, and diminished recognition of significant problems with one’s behaviors and interpersonal relationships

• Can involve cycles of relapse and remission

• Without treatment or engagement in recovery activities, addiction is progressive and can result in disability or premature death
DSM-5 Tobacco Use Disorder
4-5 Moderate, 6+ Severe

Criteria

• Tolerance
• Recurrent use resulting in failure to fulfill role obligations
• Recurrent use in hazardous situations
• Continued use despite problems
• Withdrawal or use to avoid withdrawal
  • In early remission: abstinence at least 3, but less than 12 months
  • In sustained remission: abstinence of 12 months or longer

DSM-5, American Psychiatric Association, June 2013
DSM-5 Tobacco Use Disorder
4-5 Moderate, 6+ Severe

- Using more or longer than intended
- Persistent desire or unsuccessful attempts to cut down or control
- Great deal of time spent obtaining or using
- Important activities given up to use
- Continued use despite knowledge of problems caused by use
- Craving, or strong urge/desire to use
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“A chronic disease model recognizes the long-term nature of the disorder with an expectation that patients may have periods of relapse and remission.” (US Dept of Health and Human Services, 2008)
Situations and Coping Skills

“Relapse occurs at the intersection of a triggering situation and a deficient coping response”

~Marlatt and Gordon
Relapse Prevention: Background

- Most relapse-prone period is first 3-7 days after quitting \( \text{Zhu & Pierce (1995)} \)

- Staying quit during the first week is a positive predictor of long-term abstinence

- Risk of relapse declines with each successive year of abstinence;
  - stabilizes around 10% at 30 years

Garcia-Rodrigueza, O. et. al (2013). Probability and predictors of relapse to smoking; Results of the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC). *Drug and Alcohol Dependence*. 132, 470-485
Abstinence & Relapse

- Variables with higher **abstinence** rates
  - High motivation
  - Ready to Change
  - Moderate to High Self-Efficacy
  - Supportive Social Network

- Variables with higher **relapse** rates
  - Length of previous abstinence: < 1 month
  - Unable to achieve target quit date
  - History of serious mental illness
  - History of substance abuse
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Indications of Higher Dependence

- Amount: > 20 cigarettes/day; > 3 tins/week
- Smokes/dips within 30 minutes of waking
- Withdrawal symptoms within hours of abstinence
Tobacco Specific Assessments

• Fagerstrom for smoking and smokeless
Scoring of the Fagerstrom


Classification of dependence:

0-2  Very low
3-4  Low
5    Moderate
6-7  High
8-10 Very high
Smokeless Tobacco Nicotine “Content”

- 4.8 mg nicotine/gm of moist snuff x 30 gm/can = 144 mg
- 144 mg nicotine/(1.8 mg nicotine/cigarette) = 80 cigarettes
- 80 cigarettes/(20 cigarettes/pack) = 4 packs
- 1 can snuff = 4 packs of cigarettes
- ST Users are exposed to as much, and possibly more, daily nicotine than cigarette smokers
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Treating Tobacco Dependence in a Medical Setting
Best Practices

• USPHS Guideline (www.ahrq.gov)
• Behavioral, addictions, pharmacologic treatment, and relapse prevention
• Neurobiology of tobacco dependence
• Learning opportunity
• Telephone quitlines
• Public policy
  • Taxes and smoke-free workplaces

Hurt RD, et al CA 59:314,2009
Basic Concepts

• Treat tobacco dependence for the serious medical problem it is
• Motivational counseling plus pharmacotherapy
• Dose response to counseling
• Pharmacotherapy
  • Tailored - not “one size fits all”
  • Combination therapy
  • Longer treatment duration
USPHS Clinical Practice Guideline
Pharmacotherapy

• First line
  • nicotine gum
  • nicotine patches
  • nicotine nasal spray
  • nicotine inhaler
  • nicotine lozenge
  • bupropion
  • varenicline

• Second line
  • clonidine
  • nortriptyline

www.ahrq.gov
Pharmacotherapy
Menu of Options – Long-acting Options

Nicotine patch

Bupropion (Zyban®, Wellbutrin)

Varenicline (Chantix™)
Pharmacotherapy
Menu of Options – Short-acting Options

Nicotine inhaler
Nicotine nasal spray
Nicotine gum
Nicotine lozenge - Mini lozenge
Smoking Produces Much Higher Nicotine Levels and Much More Rapidly than NRT

NRT Length of Therapy

• Most patients want to stop NRT too soon
• “Give me 6 months with the meds”
• We cannot predict who will have better outcomes with longer treatment
• Assess relapse risk
  • If increased, extend the time on meds and counseling
Abruptly Quitting vs Reduce-to-Quit (using medication with both)

Abruptly quitting

• No change or reduction in tobacco consumption and then suddenly stopping and adding smoking cessation medications

Reduce-to-quit

• While using medications gradually reducing the consumption of tobacco until being able to segue to abstinence
Research suggests that neither method (abruptly quitting or reduce-to-quit) was superior over the other.

- Since one method is not vastly better than the other, patients have the choice to decide what option is of most interest to them.
How can this be beneficial for patients

- Potentially reducing anxiety over quitting smoking
- Allowing the patient to have more autonomy
How to practice reduce-to-quit method

• Scheduled smoking reduction leading to target quit date

• Behavioral support for navigating triggers & urges and making routine changes

• Discuss medication option
  • 3 long acting & 4 short acting (encourage combination medication approach)
  • Patient can use any of the medications to hopefully allow for a success reduce-to-quit outcome
Choosing Medications

• Other than an adverse medical reactions or exclusion criteria – A patient can pick whatever medication they are most interested in trying

• Patients can start “experimenting” with the products and will hopefully discover the benefits and in turn increase confidence
Even for people that have no intention to quit smoking research shows that gradual reduction and NRT in combination have increased the likelihood of abstinence

(Cheung, Lam, Leung, Abdullah & Chan)
Nicotine Preloading

- **What is nicotine preloading** – using nicotine replacement therapy (NRT) prior to a quit date while smoking normally (no reduction in tobacco consumption)

- A study out of the UK, with 1792 participates

- The aim was to reduce the drive to smoke, thereby reducing cravings for smoking after quit day, which is the main cause for relapse

- The intervention group wore 21mg nicotine patches for 4 weeks vs a placebo patch
• The study found that active NRT increased quitting, mainly in that it reduced urges to smoke and helped participants to reduce smoking prior to quit

• After quitting the intervention group has more manageable urges to smoke

• The take away message  
  Preloading works & more research is needed

(Aveyard, Lindson, Tearne, Adams, Ahmed & Alekna)
Effect of Varenicline on Smoking Cessation Through Smoking Reduction
A Randomized Clinical Trial

Jon O. Ebbert, MD, MSc; John R. Hughes, MD; Robert J. West, PhD; Stephen I. Rennard, MD; Cristina Russ, MD; Thomas D. McRae, MD; Joan Treadow, RN, BSN; Ching-Ray Yu, PhD; Michael P. Dutro, PharmD; Peter W. Park, PhD

Conclusions

Among cigarette smokers not willing or able to quit within the next month but willing to reduce cigarette consumption and make a quit attempt at 3 months, use of varenicline for 24 weeks compared with placebo significantly increased smoking cessation rates at the end of treatment, and also at 1 year. Varenicline offers a treatment option for smokers whose needs are not addressed by clinical guidelines recommending abrupt smoking cessation.
Varenicline for smoking reduction

• RCT 24 week treatment and 28 week followup
• 1510 smokers not willing or able to quit within the next month randomized to VAR vs. placebo
• Willing to reduce smoking and make a quit attempt within next 3 months
• Intervention: 24 weeks of Varenicline vs. placebo with target reduction 50% by 4 weeks, 75% by 8 weeks and quit attempt by 12 weeks

• Ref:Ebbert et al, JAMA, 2015 Feb. 17:313 (7)
It is a Disease

• “Not a bad person with a bad habit, but a good person with a difficult disease”

– Tom Gauvin, NDC counselor
Resources


• Chueng Y, Lam T, Leung D, Abdullah A, Chann S. Nicotine replacement therapy to aid gradual cessation in smokers with no intention to quit: Association between reduction quantity and later abstinence:


• Lindson-Hawley N, Shinkins B, West R, Michie S, Aveyard P. Does cigarette reduction while using nicotine replacement therapy prior to a quit attempt predict abstinence following quit date?: Addiction, 111, 1275-1282

• Lindson-Hawley N, Aveyard P, Hughes JR. Reduction versus abrupt cessation in smokers who want to quit (review). The Cochrane Collaboration. 2012, issue 11
Questions & Discussion